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Paper No.:____

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Inventor: Dong HUANG and Dong Feng QI

Title: **NOVEL AGLYCON DAMMARANE SAPOGENINS, THEIR USE AS ANTI-CANCER AGENTS, AND A PROCESS FOR PRODUCING SAME**

Serial No.: 09/910,887

Filed: 24 July 2001

Date: 16 October 2001

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To: Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT
[Form PTO-1449 (Modified)]

United States Patent Documents

Examiner	ID	Patent No.	Issue Date	Inventor(s)	Class	Sub-Class	Filing Date
	AA	4,157,894	June 12/79	Bambardelli	2 3	230R	
SCOZ	AB	5,919,770	July 6/99	Hideo et al.	514	26	
	AC	4,621,137	Nov. 4/86	Miyake et al.	536	5-	
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

Foreign Patent Documents

Examiner	ID	Publn. No.	Publn. Date	Country/Inventor	Class	Sub-Class	Translation?
SCOZ	BA	8-208688	Aug. 13/96	Japan - Keizo et al.			NO
	BB	11-295310	Oct. 29/99	Japan - Hiroyuki et al.			NO

SOM	BC	WO/97/31933	Sept. 4/97	PCT - Cheil Je Dang Co.			
	BD						
	BE						
	BF						
	BG						
	BH						
	BI						
	BJ						
	BK						

Other Art

Examiner	ID	Author, Title, Date, Pertinent Pages, etc.
	CA	Y.S. Kim, et al., Ginsenoside Rh2 and Rh3 induce differentiation of HL-60 cells into granulocytes: modulation of protein kinase C isoforms during differentiation by ginsenoside Rh2, *The International Journal of Biochemistry & Cell Biology* 30 (1998) 327-338.
SOM	CB	A.S. Attele, et al., Ginseng Pharmacology: Multiple Constituents and Multiple Actions, *Biochemical Pharmacology*, Vol. 58, pp. 1685-1693, 1999.
	CC	H. Hasegawa, et al., Reversal of Daunomycin and Vinblastine Resistance in Multidrug-Resistant P388 Leukemia *in vitro* through Enhanced Cytotoxicity by Triterpenoids, *Planta Med.* 61 (1995) 409-413.
	CD	*www.herbmed.org/herbs/panax.htm*, Alternative Medicine Foundation - information regarding ginseng.
	CE	Abstract - Y.N. Lee, et al., In vitro induction of differentiation by ginsenoides in F9 teratocarcinoma cells, *Eur. J. Cancer* 1996, July; 32A(8):1420-8.
	CF	Abstract - S. Odashima, et al., Control of phenotypic expression of cultured B16 melanoma cells by plant glycosides, *Cancer Res.* 1985 June; 45(6):2781-4.
	CG	Abstract - L.J. Xia & R. Han, [Differentiation of B16 melanoma cells induced by ginsenoside RH2], *Yao Hsueh Hsueh Pao* 1996;31(10):742-5.
	CH	Abstract - Y. Kikuchi, et al., Inhibition of human ovarian cancer cell proliferation in vitro by ginsenoside Rh2 and adjuvant effects to cisplatin in vivo, *Anticancer Drugs* 1991 Feb;2(1):63-7.
	CI	Abstract - K.Y. Lee, et al., Ginsenoside-Rh2 blocks the cell cycle of SK-HEP-1 cells at the G1/S boundary by selectively inducing the protein expression of p27kip1, *Cancer Lett.* 1996 Dec 20; 110(1-2):193-200.
	CJ	Abstract - M. Oh, et al., Anti-proliferating effects of ginsenoside Rh2 on MCF-7 human breast cancer cells, *Int. J. Oncol.* 1999 May; 14(5):869-75.
	CK	Abstract - T. Ota, et al., G1 phase-specific suppression of the Cdk2 activity by ginsenoside Rh2 in cultured murine cells, *Life Sci.* 1997; 60(2):PL39-44.
	CL	Abstract - H. Nakata, et al., Inhibitory effects of ginsenoside Rh2 on tumor growth in nude mice bearing human ovarian cancer cells, *Jpn. J. Cancer Res.* 1998 July; 89(7):733-40.

#3

	CM	Abstract - H.E. Kim, et al., Ginsenoside RH-2 induces apoptotic cell death in rat C6 glioma via a reactive oxygen- and caspase-dependent but Bcl-X(L)-independent pathway, *Life Sci.* 1999; 65(3):PL33-40.
	CN	Abstract - J.A. Park, et al., Activation of caspase-3 protease via a Bcl-2-insensitive pathway during the process of ginsenoside Rh2-induced apoptosis, *Canc. Lett.* 1997 Dec 16; 121(1):73-81.
	CO	Abstract - K. Shinkai, et al., Inhibition of in vitro tumor cell invasion by ginsensoside Rg3, *Jpn. J. Cancer Res.* 1996 Apr. 87(4):357-62.
	CP	Abstract - H. Iishi, et al., Inhibition by ginsenoside Rg3 of bombesin-enhanced peritoneal metastasis of intestinal adenocarcinomas induced by azoxymethane in Wistar rats, *Clin. Exp. Metastasis* 1997 Nov; 15(6):603-11.
	CQ	Abstract - M. Mochizuki et a., Inhibitory effect of tumor metastasis in mice by saponins, ginsenoside-Rb2, 20(R)- and 20(S)-ginsenoside-Rg3, of red ginseng, *Biol. Pharm. Bull.* 1995 Sep.;18(9):1197-202.
	CR	Abstract - Lee, S.J., et al., Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin, *Cancer Lett.* 1999 Sep. 20; 144(1):39-43.
	CS	Abstract - M. Yoshikawa, et al., Bioactive saponins and glycosides. XI. Structures of new dammarane-type triterpene oligoglycosides, quinquenosides I, II, III, IV, and V, from American ginseng, the roots of Panax quinquefolium L., *Chem. Pharm. Bull.* (Tokyo) 1998 Apr.; 46(4):647-54.
	CT	Abstract - A.M. Popov, et al., [Comparative study of anti-tumor activity of the monoglucosides protopanaxadiol and betulafolientriol], *Antibiot. Khimioter* 1994 Jul.;39(7):24-9.
	CU	Abstract - T. Kaku et al., Chemico-pharmacological studies on saponins of Panax ginseng C.A. Meyer. II. Pharmacological Part, *Arzneimittelforschung* 1975 Apr.; 25(4):539-47.
	CV	Abstract - Y.S. Kim, et al., Ginsenoside Rh2 and Rh3 induce differentiation of HL-60 cells into granulocytes:modulation of protein kinase C isoforms during differentiation by ginsenoside Rh2, *Int. J. Biochem. Cell Biology* 1998 Mar.;30(3):327-38.
	Cw	Abstract - Y. Takino, [Studies on the pharmacodynamics of ginsenoside-Rg1,-Rb1 and -Rb2 in rats], *Yakugaku Zasshi* 1994 Aug.;114(8):550-64. (Also list of titles of related articles.)
	CX	Abstract - N.M. Duc, et al., Saponins from Vietnamese ginseng, Panax vietnamensis Ha et Grushv. collected in central Vietnam. III. *Chem. Pharm. Bull.* (Tokyo) 1994 Mar.;42(3):634-40.
	CY	Abstract - N.I. Baek, et a., Ginsenoside Rh4, a genuine dammarane glycoside from Korean red ginseng. *Planta Med.* 1996 Feb.;62(1):86-7.
	CZ	Abstract - M. Yoshikawa, et al., Bioactive saponins and glycosides. VIII. Notoginseng (1): new dammarane-type triterpene oligoglycosides, notoginsensosides-A, -B, -C and -D, from the dried root of Panax notoginseng (Burk.) F.H. Chen. *Chem. Pharm. Bull.* (Tokyo) 1997 June;45(6):1039-45.
	DA	Abstract - D. Hou, et al., Separation and determination of chemical constituents in the volatile oil of three traditional Chinese crude drugs, *J. Pharm. Biomed. Anal.* 1998 Sept.;17(8):1423-6.
	DB	Abstract - J.P. Hou, The chemical constituents of ginseng plants, *Comp. Med. East West* 1977 Summer;5(2):123-45.

#3

	DC	Absract - J.F. Cui, et al., Gas chromatographic-mass spectrometric determination of 20(S)-protopanaxadiol and 20(S)-protopanaxatriol for study on human urinary excretion of ginsenosides after ingestion of ginseng preparations, *J. Chromatogr. B. Biomed. Sci. App.* 1997 Feb. 21;689(2):349-55.
	DD	Abstract - J.F. Cui, et al., Analysis of ginsenosides by chromatography and mass spectrometry: release of 20 S-protopanaxadiol and 20 S-protopanaxatriol for quantitation, *Anal. Biochem.* 1993 May 1;210(2):411-7.
	DE	Absract - T. Ota, et al., Mechanism of action of ginsenoside Rh2: uptake and metabolism of ginsenoside Rh2 by cultured B16 melanoma cells, *J.Pharm. Sci.* 1991 Dec.;80(12):1141-6.
	DF	Abstract - C. Wakabayashi, et al., An intestinal bacerial metabolite of ginseng protopanaxadiol saponins has the ability to induce apoptosis in tumor cells, *Biochem. Biophys. Res. Commun.* 1998 May 29;246(3):725-30.
	DG	Abstract - C. Wakabayashi, et al., In vivo antimetastic action of ginseng protopanaxadiol saponins is based on their intestinal bacterial metabolites after oral administration. *Oncol. Res.* 1997;9(8):411-7.
	DH	Abstract - S.J. Lee, et al., Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin, *Cancer Lett.* 1999 Sep. 20;144(1):39-43.
	DI	Abstract - H. Hasegawa & M. Uchiyama, Antimetastatic efficacy of orally administered ginsenoside Rb1 in dependence on intestinal bacterial hydrolyzing potential and significance of treatment with an active bacterial metabolite, *Planta Med.* 1998 Dec.;64(8):696-700.
SQ	DJ	Abstract - K. Okita, et al., Anti-growth effects with components of Sho-saiko-to (TJ-9) on cultured human hepatoma cells, *Eur. J. Cancer Prevention* 2(2):169-75, 1993 Mar.
	DK	Abstract - A.S. Attele, et al., Ginseng pharmacology: multiple constituents and multiple actions, *Biochemical Pharmacology*. 58(11):1685-93, 1999 Dec. 1.
	DL	Abstract - M. Oh, et al., Anti-proliferating effects of ginsenoside Rh2 on MCF-7 human breast cancer cells, *International Journal of Oncology*, 14(5):869-75, 1999 May.
	Dm	Abstract - J. Molnar, et al., Membrane associated antitumor effects of crocine-, ginsenoside- and cannabinoid derivatives, *Anticancer Research* 20(2A):861-7, 2000 Mar.-Apr.
	DN	Abstract - M. Mochizuki, et al., Inhibitory effect of tumor metastasis in mice by saponins, ginsenoside-Rb2, 20(R)- and 20(S)-ginsenoside-Rg3 of red ginseng, *Biological & Pharmaceutical Bulletin*, 18(9):1197-202, 1995 Sep.
	DO	*www.rxlist.com/cgi/alt/ginseng.htm* - article regarding ginseng.
	DP	*online.daylight.com* - print-outs showing chemical structures of panaxadiol, protopanaxadiol, protopanaxatriol, 20(R)-ginsenoside-h2, 20(S)-ginsenoside-Rh2, Dammara-20,24-dien-3beta-ol and Betalafolien(e)triol.
	DQ	

Examiner: SABIHA QAZI

Date Considered: 9/6/2002 (09/910,887)

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.